

Application No.: 09/847,960  
Amendment and Response dated August 4, 2003  
Reply to Restriction Requirement dated July 2, 2003

Group Art Unit: 1639

**Amendments to the Claims begin on page 3**


**Remarks begin on page 7**


**Response to Restriction Requirement begins on page 8**


**Amendments to the Claims**

This listing of the claims will replace all prior versions, and listings, of claims in this application.

**Listing of Claims**

- 
1. (currently amended) A method of screening for candidate agents capable of modulating germline transcription, comprising:
    - a) adding a library of candidate agents to a plurality of cells;
    - b) preparing mRNA from said plurality of cells to form an mRNA mixture;
    - c) adding to said mixture at least a first RNase protection probe (RPP) substantially complementary to a first germline mRNA from an immunoglobulin heavy chain gene locus to form a first hybridization complex between said first germline mRNA and said first RPP;
    - d) adding an RNase protection enzyme (RPE) to said mixture, such that mRNA that is not protected is digested;
    - e) quantifying the amount of said first germline mRNA as compared to a cell in the absence of a candidate agent; and
    - f) identifying at least one candidate agent that alters the amount of said first germline mRNA.
  2. (original) A method according to claim 1, further comprising stimulating said cells to produce germline mRNA.
  3. (original) A method according to claim 1, wherein said RPP is labeled.
  4. (original) A method according to claim 3, wherein said label is a fluorescent label.
  5. (original) A method according to claim 3, wherein said label is a radioisotope.

- 
6. (original) A method according to claim 1, wherein said germline mRNA is Ig alpha-1.
  7. (original) A method according to claim 1, wherein said germline mRNA is Ig alpha-2.
  8. (original) A method according to claim 1, wherein said germline mRNA is Ig epsilon.
  9. (original) A method according to claim 1, wherein said germline mRNA is Ig gamma-1.
  10. (original) A method according to claim 1, wherein said germline mRNA is Ig gamma-2.
  11. (original) A method according to claim 1, wherein said germline mRNA is Ig gamma-3.
  12. (original) A method according to claim 1, wherein said germline mRNA is Ig gamma-4.
  13. (original) A method according to claim 1, wherein said RPP has a sequence selected from the group consisting of the sequences depicted in Figure 3.
  14. (original) A method according to claim 1, wherein said RPP has a sequence selected from the group consisting of the sequences depicted in Figure 4.
  15. (original) A method according to claim 1, wherein said library comprises at least  $10^3$  candidate agents.
  16. (original) A method according to claim 1, wherein said library comprises at least  $10^5$  candidate agents.

- 
17. (original) A method according to claim 1, further comprising:
- a) adding to said mixture at least a second RNase protection probe (RPP) substantially complementary to a second germline mRNA to form a second hybridization complex between said second germline mRNA and said second RPP;
  - b) quantifying the amount of said second germline mRNA as compared to a cell in the absence of a candidate agent; and
  - c) identifying at least one candidate agent that alters the amount of said first germline mRNA but not said second germline mRNA.
18. (original) A method according to claim 1, wherein said library comprises small molecules.
19. (original) A method according to claim 1, wherein said library comprises peptides.
20. (original) A method according to claim 19, wherein said peptides are random peptides.
21. (original) A method according to claim 19, wherein said peptides are partially random peptides.
22. (original) A method according to claim 19, wherein said adding is done using retroviruses encoding said peptides.
23. (original) A method according to claim 19 wherein said adding is done using retroviruses comprising sequence derived from a cDNA library.
24. (original) A method of quantifying the amount of a plurality of germline constructs comprising:
- a) preparing mRNA from said plurality of cells to form an mRNA mixture;

- c) adding at least three RNase protection probes (RPPs) selected from the group consisting of the sequences depicted in Figures 3 and 4;
- d) adding an RNase protection enzyme (RPE) to said mixture, such that mRNA that is not protected is digested;
- e) quantifying the amount of said germline mRNA.

B1  
Cmt

25. (original) A kit for quantifying the amount of germline mRNA in a sample, comprising
- a) at least one RNase protection probe (RPP) comprising a nucleic acid sequence selected from the group consisting of the nucleic acid sequences of the Ig $\alpha$ 1, Ig $\alpha$ 2, Ig-epsilon, Ig gamma-1, Ig gamma-2, Ig gamma-3 and Ig gamma-4 RPPs set forth in Figures 3 and 4; and
  - b) an RNase protection enzyme (RPE);  
and optionally comprising at least one RNase protection probe (RPP) which is substantially complementary to a transcript of a housekeeping gene.

26. (original) A kit according to claim 25, wherein all RNase protection probes are labeled.
-